

EXHIBIT 15



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Cabilly et al.

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(54) METHODS OF PRODUCING IMMUNOGLOBULINS, VECTORS AND TRANSFORMED HOST CELLS FOR USE THEREIN	4,792,447 A 12/1988 Uhr et al. 4,816,567 A 3/1989 Cabilly et al. 4,965,196 A 10/1990 Levinson et al. 5,081,235 A 1/1992 Shively et al. 5,098,833 A 3/1992 Lasky et al. 5,116,964 A 5/1992 Capon et al. 5,137,721 A 8/1992 Dallas 5,179,017 A 1/1993 Axel et al. 5,225,538 A 7/1993 Capon et al. 5,336,603 A 8/1994 Capon et al. 5,420,020 A 5/1995 Riggs 5,428,130 A 6/1995 Capon et al. 5,455,165 A 10/1995 Capon et al. 5,500,362 A 3/1996 Robinson et al. 5,514,582 A 5/1996 Capon et al. 5,561,053 A 10/1996 Crowley 5,583,013 A 12/1996 Itakura 5,585,089 A 12/1996 Queen et al. 5,605,689 A 2/1997 Ammann 5,612,185 A 3/1997 Uhr et al. 5,648,237 A 7/1997 Carter 5,686,072 A 11/1997 Uhr et al. 5,721,108 A 2/1998 Robinson et al. 5,736,137 A 4/1998 Anderson et al. 5,807,715 A 9/1998 Morrison et al. 5,840,545 A 11/1998 Moore 5,846,818 A 12/1998 Robinson et al. 5,877,293 A 3/1999 Adair et al. 5,965,405 A 10/1999 Winter 5,997,867 A 12/1999 Waldmann et al. 6,054,297 A 4/2000 Carter et al. 6,054,561 A 4/2000 Ring 6,120,767 A 9/2000 Robinson et al. 6,204,023 B1 3/2001 Robinson et al. 6,331,415 B1 12/2001 Cabilly et al. 6,455,275 B1 9/2002 Axel et al. 6,548,640 B1 4/2003 Winter
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(52) U.S. Cl. 435/69.6 ; 435/252.1; 435/252.3; 435/252.33; 435/254.11; 435/254.2; 435/254.21; 435/69.7; 435/70.21; 435/71.2; 435/71.1; 435/70.1; 435/320.1; 435/455; 435/483; 435/485; 435/471; 435/69.1	
(58) Field of Classification Search None See application file for complete search history.	
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Primary Examiner—Padmashri Ponnaluri**(57) ABSTRACT**

The invention relates to processes for producing an immunoglobulin or an immunologically functional immunoglobulin fragment containing at least the variable domains of the immunoglobulin heavy and light chains. The processes can use one or more vectors which produce both the heavy and light chains or fragments thereof in a single cell. The invention also relates to the vectors used to produce the immunoglobulin or fragment, and to cells transformed with the vectors.

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EX PARTE
REEXAMINATION CERTIFICATE
ISSUED UNDER 35 U.S.C. 307

THE PATENT IS HEREBY AMENDED AS
INDICATED BELOW.

Matter enclosed in heavy brackets [] appeared in the
patent, but has been deleted and is no longer a part of the
patent; matter printed in italics indicates additions made
to the patent.

AS A RESULT OF REEXAMINATION, IT HAS BEEN
DETERMINED THAT:

The patentability of claims 1-20 and 33-36 is confirmed. 15

Claims 21, 27 and 32 are determined to be patentable as
amended.

Claims 22-26 and 28-31, dependent on an amended 20
claim, are determined to be patentable.

21. A method comprising

a) preparing a *first* DNA sequence [consisting essentially
of DNA] encoding an immunoglobulin [consisting of

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an immunoglobulin] heavy chain and a *second* DNA
sequence encoding an immunoglobulin light chain [or
Fab region, said immunoglobulin having specificity for
a particular known antigen];

b) inserting the DNA [sequence] *sequences* of step a) into
a replicable expression vector wherein *each sequence is*
operably linked to a suitable promoter;

c) transforming a prokaryotic or eukaryotic microbial host
cell culture with the vector of step b);

d) culturing the host cell *so that said immunoglobulin*
heavy and light chains are produced as separate mol-
ecules in said transformed host cell; and

e) recovering the immunoglobulin from the host cell
culture, said immunoglobulin being capable of binding
to a known antigen.

27. The method of claim 26 wherein the heavy chain and
light [chains or Fab region] *chain* are deposited within the
cells as insoluble particles.

32. The insoluble particles of heavy chain and light chains
[or Fab region] produced by the method of claim 27.

* * * * *